Initial Approval: July 10, 2019

CRITERIA FOR PRIOR AUTHORIZATION

Spinal Muscular Atrophy (SMA) Agents

BILLING CODE TYPE For drug coverage and provider type information, see the KMAP Reference Codes webpage.

MANUAL GUIDELINES The following drugs requires prior authorization:
Nusinersen (Spinraza®)
Onasemnogene (Zolgensma®)

CRITERIA FOR INITIAL APPROVAL FOR NUSINERSEN (Must meet the following criteria):

- Patient must have a diagnosis of spinal muscular atrophy (SMA), confirmed by SMN1 (chromosome 5q) gene mutation or deletion.[1,2] Must meet one of the following:
  - Homozygous SMN1 gene deletion or mutation (e.g., homozygous deletion of exon 7 at locus 5q13)
  - Compound heterozygous SMN1 mutation (e.g., deletion of SMN1 exon 7[allele 1] and mutation of SMN1 [allele 2])
- Provider must submit documentation the patient has a sufficient number of copies of SMN2 gene defined as ≥ 2 copies of SMN2 gene.[1,2]
- Prescribed by or in consultation with a neurologist with expertise in the diagnosis of SMA.[3]
- Prescriber must submit baseline documentation of one of the following:[5]
  - Hammersmith Infant Neurological Exam (HINE) (infant to early childhood)
  - Hammersmith Functional Motor Scale Expanded (HFMSE)
  - Upper Limb Module (ULM) Test (Non-ambulatory) or revised Upper Limb Module (RULM) Test (Non-ambulatory)
  - Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)
- Must be administered by, or under the direction of, healthcare professionals experienced in performing lumbar punctures.[5]
- Dosing must not exceed 12 mg. There are 4 loading doses. The first three loading doses should be administered at 14-day intervals. The 4th loading dose should be administered 30 days after the 3rd dose.[5]
- Zolgensma (onasemnogene) will not be prescribed concurrently with Spinraza (nusinersen) as dual therapy.
- Patient is not on permanent ventilation (≥ 16 hours/day for > 21 days in the absence of an acute reversible event or tracheostomy).[5]

LENGTH OF INITIAL APPROVAL 6 months (1 loading dose [4 injections] and 1 maintenance dose)

CRITERIA FOR RENEWAL APPROVAL FOR NUSINERSEN (Must meet the following criteria):

- The patient continues to meet initial criteria.
- Must meet one of the following:
  - Prescriber attests that the patient has achieved a new motor milestone or maintained muscle function compared to pretreatment baseline when they would otherwise be unexpected to do so (e.g., sit unassisted, stand, walk)
  - Prescriber submits post-treatment documentation with the most recent results (< 1 month prior to request) documenting a positive clinical response from pretreatment baseline status demonstrated by at least one of the following:
    - Hammersmith Infant Neurological Exam (HINE) (infant to early childhood):
      - Improvement or maintenance of previous improvement of at least 2 point (or maximal score) increase in ability to kick or Improvement or maintenance of previous improvement of at least 1-point increase in any other HINE milestone (e.g., head control, rolling, sitting, crawling, etc.),

  - Hammersmith Functional Motor Scale Expanded (HFMSE):
    - Improvement or maintenance of previous improvement of at least a 3-point increase in score from pretreatment baseline
  - Upper Limb Module (ULM) Test (Non-ambulatory) or revised Upper Limb Module (RULM) Test (Non-ambulatory)
    - Improvement or maintenance of previous improvement of at least a 2-point increase in score from pretreatment baseline
  - Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)
    - Improvement or maintenance of previous improvement of at least a 4-point increase in score from pretreatment baseline
- Dosing must not exceed 12 mg. A maintenance dose should be administered once every 4 months.[5]

LENGTH OF RENEWAL APPROVAL 12 months (3 maintenance doses)

CRITERIA FOR APPROVAL FOR ONASEMNOGENE (Must meet the following criteria):

- Patient must have a diagnosis of spinal muscular atrophy (SMA).[4]
  - Genetic testing confirms the presence of homozygous mutation in the SMN1 gene (e.g., biallelic deletions of exon 7).[4,6]
  - Genetic testing confirms that member does not have a single base substitution in SMN2 gene (c.859G>C modification on exon 7).[6]
- Prescribed by or in consultation with a neurologist with expertise in the diagnosis of SMA.[3]
- Patient must have symptoms prior to 6 months of age.[6]
- Patient must be < 2 years of age.[6]
- For patients born pre-maturely, Zolgensma (onasemnogene) cannot be administered until the corresponding full gestational age is reached.[6]
- If replacing Spinraza (nusinersen), Zolgensma (onasemnogene) will not be prescribed concurrently as dual therapy.
- Patient must not have previously received Zolgensma (onasemnogene).[6]
- Prescriber must submit baseline documentation of one of the following:
  - Hammersmith Infant Neurological Exam (HINE) (infant to early childhood)
  - Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)[6]
- Patient must have baseline laboratory tests demonstrating Anti-AAV9 antibody titers ≤ 1:50 as determined by ELISA binding immunoassay.[4,6]
- Patient must not have advanced SMA (i.e. complete paralysis of limbs, permanent ventilator dependence).[6]
- Patient must not require permanent ventilation, tracheostomy, or non-invasive ventilation beyond use for sleep (requiring invasive ventilation (tracheostomy), or respiratory assistance for 16 or more hours per day (including noninvasive ventilatory support) continuously for 14 or more days in the absence of an acute reversible illness, excluding perioperative ventilation).[6]
- Total dose must not exceed 1.1×10^{14} vector genomes (vg) per kilogram (kg).[6]

LENGTH OF INITIAL APPROVAL 1 month (1 infusion per lifetime). Reauthorization is not permitted.[6]

Table 1. Types of spinal muscular atrophy (SMA).[3]

SMA Type	Highest motor function without treatment*
1	Unable to sit independently
2	Able to sit, never able to walk independently
3	Able to walk independently

*SMA Types are classified based on the highest motor milestone attained.[3]

References:

1. Finkel, Richard S., et al. "Nusinersen versus sham control in infantile-onset spinal muscular atrophy." New England Journal of Medicine 377.18 (2017): 1723-1732. Available at https://www.nejm.org/doi/10.1056/NEJMoa1702752. Accessed 6/26/19.
2. Mercuri, Eugenio, et al. "Nusinersen versus sham control in later-onset spinal muscular atrophy." New England Journal of Medicine 378.7 (2018): 625-635.
3. Evidence in focus: Nusinersen use in spinal muscular atrophy. Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology 2018; 91:923-33. Available at https://n.neurology.org/content/91/20/923.long. Accessed on 5/31/19.
4. Mendell JR, Al-zaidy S, Shell R, et al. Single-Dose Gene-Replacement Therapy for Spinal Muscular Atrophy. N Engl J Med. 2017;377(18):1713-1722.
5. Spinraza (nusinersen) [prescribing information]. Cambridge, MA: Biogen; June 2019.
6. Zolgensma (onasemnogene abeparvovec) [prescribing information]. Bannockburn, IL: AveXis, Inc; May 2019.

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